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Rearrangements Accompanying the Fragmentation of Ionized 1-Phenylalkan-1-ols†

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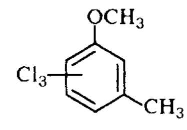
Some aspects of the fragmentation sequence of 1-phenylalkan-1-ols ($C_6H_5CH(OH)R$), which consists of the loss of $R^\bullet$ followed by the elimination of CO and subsequently of H_2, are discussed. Labelling studies and collision activation data of reference compounds allow a mechanism to be proposed for this rearrangement.

INTRODUCTION

In a note on the potential misidentification of trichlorophenylethanol in imported peppers, Cairns *et al.*[2] reported that the electron impact (EI) mass spectra of methyltrichloroanisoles (**1**) and 1-(2,4,5-trichlorophenyl) ethanol (**2**) are essentially indistinguishable. The main fragments observed in either case are $[M - {}^\bullet CH_3]^+ \rightarrow [M - {}^\bullet CH_3 - CO]^+$ with subsequent elimination of $^\bullet Cl$ and HCl. Whereas from methyl phenyl ethers loss of $^\bullet CH_3$ followed by that of CO is well known,[3] the analogous process starting from $M^{+\bullet}$ of 1-phenylethanol derivatives seemed to be unexpected. The authors showed that the OD analogue of **2** retained the label after the loss of $^\bullet CH_3$ and $^\bullet CH_3 + CO$ and that following collision activation of $M^{+\bullet}$ of **2** the ions $[M - {}^\bullet CH_3]^+$, $[M - {}^\bullet CH_3 - CO]^+$ and $[M - {}^\bullet CH_3 - CO - HCl]^+$ were formed.



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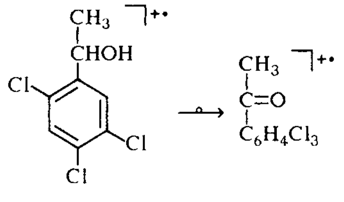


2 3

These findings suggested a rearrangement of **2** to the isomeric ketone **3**. Such rearrangements are well documented for vinyl carbinols, the migrating hydrogens being the hydroxyl- and the carbinol-H:[4,5]

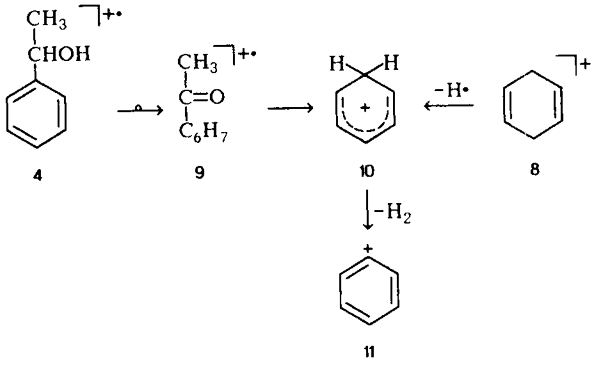
$$RCH{=}CH(CHOH)R' \rightarrow RCH_2CH_2COR' \quad (1)$$

Scattered data which suggest an analogous process for compounds comprising a benzyl alcohol moiety (2H migrating to the benzene ring) can be found,[4–8] some of which will be commented on below. Thus, Nibbering and de Boer[8] studied **4** and its deuterated analogues **5**–**7** and showed that no exchange of label occurs prior to the loss of $^\bullet CH_3$ and $CH_3CO^\bullet$ from $M^{+\bullet}$ and prior to the formation of CH_3CO^+, and that some scrambling between the hydrogen atoms except those of the methyl group accompanies the formation of $[C_6H_5]^+$ (*m/z* 77). They discussed protonated benzaldehyde and protonated tropone as possible intermediates in the path leading to $[C_6H_7]^+$ (*m/z* 79). In the following new data are presented which indicate that these species are unlikely as intermediates and a mechanism is proposed for this peculiar rearrangement (Scheme 1).

RESULTS AND DISCUSSION

The EI mass spectrum of **4** (Fig. 1) clearly shows the ions resulting from the loss of $^\bullet CH_3$ and $^\bullet CH_3 + CO$ (*m/z* 107 and 79) from $M^{+\bullet}$ (*m/z* 122). A parent ion spectrum of the *m/z* 79 ion reveals its origin from both *m/z* 107 and 122, and a daughter ion scan of the *m/z* 122 ion demonstrates it to be the precursor of *m/z* 107 and 79 ions and of small amounts of *m/z* 78, 77, 45 and 43 ions. To the direct formation of $[M - CH_3CO^\bullet]^+$ from $M^{+\bullet}$ corresponds the appearance of an ion $[CH_3CO]^+$ (*m/z* 43) in Fig. 1. Deuterium labelling (**5**, **6**, **7**) confirms the earlier observation[8] that no exchange of label occurs prior to the loss of $^\bullet CH_3$ and $CH_3CO^\bullet$ and to the formation of CH_3CO^+.

Fragmentation of unrearranged **4** explains the formation of ions of *m/z* 107 (loss of $^\bullet CH_3$), 77 ($[C_6H_5]^+$) and



Scheme 1. Fragmentation of **4**

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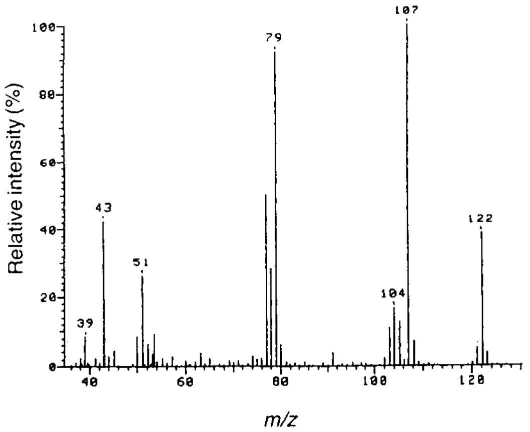
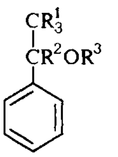


Figure 1. EI mass spectrum of 1-phenylethan-1-ol (**4**)



	R^1	R^2	R^3
5	D	H	H
6	H	D	H
7	H	H	D

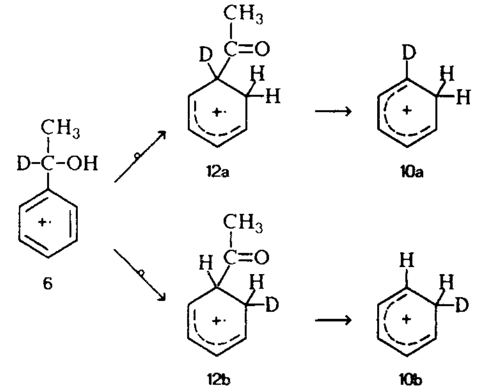
45 ($[CH_3CHOH]^+$) and also of *m*/*z* 78 ($[C_6H_6]^{+\bullet}$; loss of CH_3CHO with concomitant transfer of $H^{\bullet}$ to the ring). The formation of an *m*/*z* 43 ion ($[CH_3CO]^+$) directly from *m*/*z* 122 suggests a preceding rearrangement to **9**. For the genesis of an *m*/*z* 79 ion ($[C_6H_7]^+$) several possibilities can be considered: loss of $CH_3CO^{\bullet}$ from **4** with concomitant or from **9** with preceding migration of 2H or by the loss of CO from $[M - {}^{\bullet}CH_3]^+$ originating from **4** or from **9**. In the last case the sequence is obvious. $[M - {}^{\bullet}CH_3]^+$ from **4** corresponds to benzaldehyde protonated at the carbonyl group. The higher proton affinity of benzaldehyde (837 kJ mol^{-1}) than that of benzene (765 kJ mol^{-1}) [9] makes it probable that this species is obtained from benzaldehyde under CI conditions. The CI(CH_4) mass spectrum of benzaldehyde shows $[M + C_2H_5]^+$ 1%, $[M + H]^+$ 100%, $M^{+\bullet}$ 4%, $[M - H]^+$ 6%, $[C_6H_7]^+$ 15% and $[C_6H_6]^{+\bullet}$ 1%. Collision activation (CA) of $[M + H]^+$ (*m*/*z* 107) demonstrates that this species decomposes essentially only by formation of $[C_6H_7]^+$ (67%) and $CO^{+\bullet}$ (100%) (the only additional daughter ion is $[C_2H_2]^{+\bullet}$, 6%). In contrast, the CA spectrum of the *m*/*z* 107 ion from **4** yields $[C_6H_7]^+$ (100%) and $CO^{+\bullet}$ (10%) and in addition $[C_6H_5]^+$ (3%) and $[C_2H_2]^{+\bullet}$ (1%). This makes it unlikely that the *m*/*z* 107 ion from **4** corresponds to a major extent to protonated benzaldehyde. Protonated tropone[8] can be excluded definitively: the CI (CH_4) mass spectrum of tropone comprises the ions $[M + C_2H_5]^+$ (1%), $[M + H]^+$ (100%), $M^{+\bullet}$ (3%), $[C_6H_7]^+$ (9%) and $[C_6H_6]^{+\bullet}$ (4%). The CA spectrum of $[M + H]^+$ (*m*/*z* 107) shows preferentially hydrocarbon ions at *m*/*z* 26 (100%), 28 (42%), 30 (3%), 39 (34%), 41 (2%), 51 (6%), 53 (30%), 55 (12%) 65 (1%), 77 (26%) and 79 (18%). Hence the $[M - {}^{\bullet}CH_3]^+$ ion from **4** decomposing to $[C_6H_7]^+$ must have a structure different from protonated benzaldehyde or tropone.

Regarding the formation and structure of the *m*/*z* 79 ion ($[C_6H_7]^+$), one can go back to earlier observations[10,11] made with benzyl alcohol: it was proposed that the *m*/*z* 79 ion observed in its mass spectrum has the same structure as $[M - H^{\bullet}]^+$ from cyclohexa-1,4-diene (**8**), essentially based on the fact that in either case *m*/*z* 79 showed a pronounced loss of H_2. This supposition can be confirmed for **4**: the CA spectra of the *m*/*z* 79 ions from **4** and from **8** are indistinguishable (→*m*/*z* 77, 53, 51 and 39) (see also Ref. 12, where it is concluded that protonated benzene (**10**) is the reacting species of the *m*/*z* 79 ion). The narrow metastable peak for the transition *m*/*z* 79 → 77 from **4** corresponding in our case to a release of 2.4 kJ mol^{-1} translational energy is typical for protonated benzene.[13]

As far as the fragmentation processes leading to the *m*/*z* 79 ion and subsequently to the *m*/*z* 77 ion are concerned, some information can be obtained: parent scans of the *m*/*z* 77 and 78 ions from **4** give the following picture: the *m*/*z* 78 ion has weak precursor ions at *m*/*z* 79, 80, 104, 106, 107 and 122, and the *m*/*z* 77 ion weak precursor ions at *m*/*z* 78, 103 and 107 and slightly more abundant ones ($\leqslant 6\%$) at *m*/*z* 79 and 105. An evaluation of the peak intensities in the EI spectra (average of three recordings each from three independent measurements for **5** and **6**; the values for **7** are not included since, owing to the incomplete exchange, the spectrum of **7** obtained by subtraction is not sufficiently reliable and can therefore be used only qualitatively) gives the following picture: the CH_3 group is lost without any preceding H exchange with the rest of the molecule. The benzylic H is retained completely during the formation of the *m*/*z* 79 ion (complete shift to *m*/*z* 80 for **6**). Subsequently, H, D, H_2 and HD are lost, giving 35% $[C_6H_5]^+$, 37% $[C_6H_4D]^+$, 10% $[C_6H_6]^{+\bullet}$ and 18% $[C_6H_5D]^{+\bullet}$ of the sum of these ions after correction for ${}^{13}C$ contributions. Comparison with the relative intensities for unlabelled **4** (72% $[C_6H_5]^+$, 28% $[C_6H_6]^{+\bullet}$ after correction for ${}^{13}C$) allows the following conclusions: the abundance of $[C_6H_5D]^{+\bullet}$ (*m*/*z* 79) should be 24% if $H^{\bullet}$ was lost randomly from $[C_6H_6D]^+$ (this value is a lower limit since a primary isotope effect actually discriminates against the loss of D). As the observed value is 18% there must be an alternative route to $[C_6H_6]^{+\bullet}$ from **4** (and hence to $[C_6H_5D]^{+\bullet}$ from **6**) which comprises a preferential loss of the benzylic H prior to a randomizing rearrangement (see above the various precursors of the *m*/*z* 78 ion). Labelling data demonstrate the same effect for 1-phenylpropan-1-ol.[7]

Of greater importance in the present context is the ion at *m*/*z* 77 in the EI spectrum of **4**. For **6** the ratio of $[C_6H_5]^+$ to $[C_6H_4D]^+$ should be 2:5 for a random loss of H_2 and HD, ignoring an isotope effect which again would be in favour of the H_2 loss. The observed ratio of 35:37 deviates grossly from the calculated value (note that for $C_6H_5CD(OH)C_2H_5$ the same 1:1 ratio was observed[7]). Assuming a 1,1-elimination of H_2 [13] for the formation of **11** from **10**, a 1:1 ratio for the loss of H_2 and HD in the case of **6** implies that **10a** and **10b** are formed with comparable abundances. For undec-2-en-4-ol transfer of the carbinol-H to either of the sp^2-C during the rearrangement according to Eqn (1) was demonstrated.[4] Assuming the same process for **6**, one would actually obtain **12a** and **12b** and subsequently **10a** and **10b**, which then eliminate H_2 or HD to give $[C_6H_4D]^+$ and $[C_6H_5]^+$ (Scheme 2).

Hydrogen migrations from a side-chain to the benzene ring resulting in distonic ions are well known,[14] the rate of the transfer being governed by the



Scheme 2. Fragmentation of **6**.

dissociation energy of the transferred H and the local proton affinity of the acceptor site. In the case of alkyl phenyl carbinols the preferred donors are the benzylic C and the OH group. For toluene the proton affinity at the *ortho* is much higher than that at the *ipso* position.[15] The CH_3CHOH substituent may enhance the *ipso* transfer; in any case, the double transfer of *ortho* plus *ipso* is the most likely result and the formation of 5-acetylcyclohexa-1,3-diene (**12**) as the decomposing intermediate explains best the observed behaviour of **4** and its analogues.

Data from the literature may be commented on briefly. 1-Phenylpropan-1-ol fragments in the same way as **4** ($M^{+\cdot}$, $[M - {}^{\cdot}C_2H_5]^+$, *m/z* 79 and 77); see also above.[7] 3-Phenylprop-1-en-3-ol demonstrates a more pronounced H-migration to the vinyl group than to the benzene ring.[4] 1-*p*-Tolylethan-1-ol shows a partial loss of the label of the aromatic methyl group during the hydrogen elimination from $[CH_3C_6H_5D]^{+\cdot}$.[7] Benzyl alcohol undergoes $[M - H^{\cdot}]^+ \rightarrow [C_6H_7]^+ \rightarrow [C_6H_5]^+$, but here the picture is obscured by the competing formation of $[C_6H_7]^+$ by a loss of ${}^{\cdot}CHO$ directly from $M^{+\cdot}$ (see also above).[10,11]

EXPERIMENTAL

Mass spectra

EI and $CI(CH_4)$ spectra were obtained on a Finnigan MAT 212 instrument with a liquid sample inlet (Fig. 1) or with gas chromatography (evaluation of D shifts); the ionization energy was 70 eV. CA spectra (70 eV, collision energy 100 eV, argon, intensity reduction 50%) and metastable ion measurements were performed with an HS-Q 30 instrument (Finnigan MAT, Bremen).

^1H NMR spectra

A Bruker AM 300 instrument was used at 300 MHz, with $CDCl_3$ as solvent.

Compounds

Benzaldehyde, cyclohexa-1,4-diene and tropene were commercially available.

1-Phenlethan-1-ol (**4**) was prepared from methyl phenyl ketone by reduction with $LiAlH_4$ and purification by fractional distillation; b.p. (30 mbar) 96–97 °C; ^1H NMR, δ (ppm) 1.46, d (J = 6.4 Hz) (3H), 2.44, s (1H), 4.83, q (J = 6.4 Hz) (1H), ~7.30, m (5H).

[1-^2H]-1-Phenylethan-1-ol (**6**) was obtained analogously to **4** using $LiAlD_4$. Isotopic purity 98%. ^1H NMR, δ (ppm) 1.45, s (3H), 2.76 s (1H), ~7.35, m (5H).

[*O*-^2H]-1-Phenylethan-1-ol (**7**) was prepared from **4** by exchange with D_2O. According to the EI spectrum, 30% of the OD compound could be obtained mainly due to back-exchange in the mass spectrometer. By subtraction of the mass spectrum of **4**, that of **7** could be calculated.

Trideuteromethyl phenyl ketone (acetophenone-d_3) was prepared by refluxing acetophenone (5 g) with a solution of 11.5 g of Na in 50 cm^3 of D_2O for 72 h. After extraction with diethyl ether and the usual work-up, deuterated acetophenone was obtained (90% d_3, 10% d_2 by NMR and EIMS).

[2,2,2-$^2H_3$]-1-Phenylethan-1-ol (**5**) was prepared by reduction of acetophenone-d_3 with $LiAlH_4$. ^1H NMR, δ (ppm) 1.45, s (0.1 H from the d_2 compound), 2.56, s (1H), 4.81, s (1H), ~7.33, m (5H).

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